

Support Dr. Burkhardt's Research: Precision Pancreatic Cancer Care through Personalized Models of Disease

Problem: Pancreatic cancer is a unique clinical problem. Despite improvements in the past two decades for patients with other cancer types, outcomes in pancreas cancer remain poor. Pancreas cancer kills nearly 50,000 patients per year and is currently the third most common cause of cancer death in the United States. Unfortunately, rates of pancreas cancer are rising and the number of new patients in 2030 will be 50% higher than the number in 2010 [1]. Nearly 20% of patients are eligible for a potentially curative surgery, however, many of these patients have recurrent disease due to a failure of chemotherapy to control microscopic disease.

“Traditional” Therapy: In patients who undergo resection, research at Johns Hopkins has proven that chemotherapy given after surgery (i.e. “adjuvant therapy”) reduces the chance of disease recurrence [2]. There are several chemotherapeutic drugs to choose from in pancreas cancer. But unlike in breast cancer, where the subtype of cancer determines the best drug regimen, the traditional method of treating pancreas cancer does not account for disease subtype. Rather than prescribing the best drug(s) for each patient’s unique cancer, all patients with pancreas cancer often receive the same regimen. This “traditional” therapy does not efficiently draw on the collective expertise of the health system or pancreas cancer researchers.

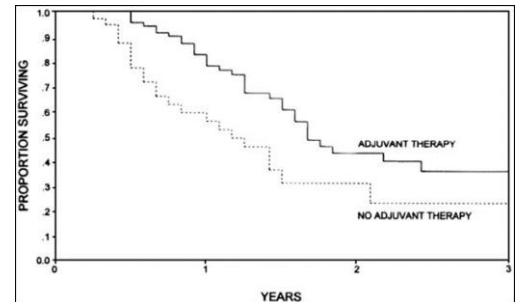


Figure 1: Adjuvant therapy improves survival after surgery for pancreas cancer.



Figure 2: A patient's cancer growing 3 days after surgery.

Precision Pancreatic Cancer Care: We propose a model of care whereby each patient’s tumor is studied to identify the best drug(s) for their individual cancer. While the patient recovers from surgery, their cancer is grown in a research laboratory as a tumor “organoid” for molecular study and precision testing [3]. The testing for each patient’s tumor will include direct sensitivity analysis for the drugs used in traditional therapy, genetic testing to identify key cancer susceptibilities (such as BRCA mutations) and next-generation testing using RNA-seq to subtype each patient’s cancer [4]. When the patient is ready for chemotherapy, data gathered from these molecular studies will be discussed at a multidisciplinary meeting of clinician-scientists and the optimal regimen for each patient can be selected.

The Next Steps: While the unique sensitivity for some tumors are known, there are many tumors for which the best drug is unknown. This work will help to clarify which tumors respond best to each drug and will help determine which molecular tests are most helpful in our patients. All the while, patients diagnosed today may benefit from the practical application of our most promising science. Finally, new discoveries and novel drugs that are currently in development can be rapidly integrated into this translational research program.

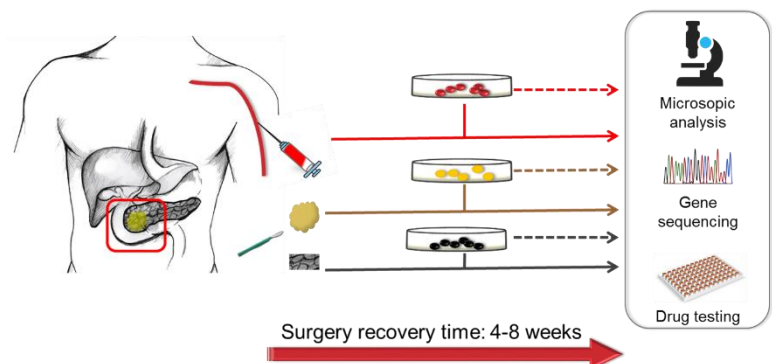


Figure 3: As personal models of cancer, organoids (shown growing as spheres in red, yellow, and black) allow for next-generation testing to be completed that help physicians select the best chemotherapy.

(1) Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. *Cancer Res* 2014 Jun 1;74(11):2913-2921. (2) Yeo CJ, Abrams RA, Grochow LB, Sohn TA, Ord SE, Hruban RH, et al. Pancreaticoduodenectomy for pancreatic adenocarcinoma: postoperative adjuvant chemoradiation improves survival. A prospective, single-institution experience. *Ann Surg* 1997 May;225(5):621-33; discussion 633-6. (3) Boj SF, Hwang CI, Baker LA, Chio II, Engle DD, Corbo V, et al. Organoid models of human and mouse ductal pancreatic cancer. *Cell* 2015 Jan 15;160(1-2):324-338. (4) Bailey P, Chang DK, Nones K, Johns AL, Patch AM, Gingras MC, et al. Genomic analyses identify molecular subtypes of pancreatic cancer. *Nature* 2016 Mar 3;531(7592):47-52.